CLAIMS

We Claim:

1. An antimicrobial sulfonamide derivative, or a salt or a hydrate thereof, comprising:

a core cyclic peptide or core antibiotic of a lipopeptide antibiotic; and

a lipophilic moiety,

wherein said lipophilic moiety is covalently attached to the core cyclic peptide or core cyclic antibiotic *via* a linking chain which includes a sulfonamide linkage.

2. The antimicrobial sulfonamide derivative, salt or hydrate of Claim 1 in which the linking chain is a sulfonamide linkage.

3. The antimicrobial sulfonamide derivative, salt or hydrate of Claim 1 in which the linking chain is a linker that links the core cyclic peptide or core antibiotic to the lipophilic moiety.

4. The antimicrobial sulfonamide derivative, salt or hydrate of Claim 1 which is a compound according to structural Formula (I):

(I) $Y—X—N(R^4)(—L—X—N(R^1))_m—R$

wherein:

Y is a lipophilic moiety;

Each X is independently selected from the group consisting of —CO— —SO_2—, —CS—, —PO—, —OP(O)—,—OC(O)—, —NHCO— and —$N(R^1)$CO— with the proviso that at least one X is —SO_2—;

m is 0 or 1;

L is a linker;

N is nitrogen;

R^1 and R^4 are each independently selected from the group consisting of hydrogen, (C_1-C_{25}) alkyl optionally substituted with one or more of the same or different R^2

groups, (C_1-C_{25}) heteroalkyl optionally substituted with one or more of the same or different R^2 groups, (C_5-C_{30}) aryl optionally substituted with one or more of the same or different R^2 groups, (C_5-C_{30}) arylaryl optionally substituted with one or more of the same or different R^2 groups, (C_5-C_{30}) biaryl optionally substituted with one or more of the same or different R^2 groups, five to thirty membered heteroaryl optionally substituted with one or more of the same or different R^2 groups, (C_6-C_{30}) arylalkyl optionally substituted with one or more of the same or different R^2 groups and six to thirty membered heteroarylalkyl optionally substituted with one or more of the same or different R^2 groups;

each R^2 is independently selected from the group consisting of —OR^3, —SR^3, —NR^3R^3, —CN, —NO_2, —N_3, —$C(O)OR^3$, —$C(O)NR^3R^3$, —$C(S)NR^3R^3$, —$C(NR^3)NR^3R^3$, —CHO, —R^3CO, —SO_2R^3, —SOR^3, —$PO(OR^3)_2$, —$PO(OR^3)$, —CO_2H, —SO_3H, —PO_3H, halogen and trihalomethyl;

each R^3 is independently selected from the group consisting of hydrogen, (C_1-C_6) alkyl, (C_5-C_{10}) aryl, five to sixteen membered heteroaryl, (C_6-C_{16}) arylalkyl and six to sixteen membered heteroarylalkyl; and

R is a core cyclic peptide or core antibiotic of a lipopeptide antibiotic.

5. The antimicrobial sulfonamide derivative of Claim 4 in which R is the core cyclic peptide of laspartomycin, zaomycin, crystallomycin, aspartocin, amphomycin, glumamycin, brevistin, cerexin A, cerexin B, Antibiotic A-30912, Antibiotic A-1437, Antibiotic A-54145, Antibiotic A-21978C or tsushimycin.

6. The antimicrobial sulfonamide derivative of Claim 4 in which R is the core antibiotic of laspartomycin, zaomycin, crystallomycin, aspartocin, amphomycin, glumamycin, brevistin, cerexin A, cerexin B, Antibiotic A-30912, Antibiotic A-1437, Antibiotic A-54145, Antibiotic A-21978C or tsushimycin.

7. The antimicrobial sulfonamide derivative of Claim 4 in which R is the core cyclic peptide of laspartomycin, aspartocin, Antibiotic A-30912, Antibiotic A-1437, Antibiotic A-54145 or Antibiotic A-21978C.

8. The antimicrobial sulfonamide derivative of Claim 4 in which R is the core

antibiotic of laspartomycin, aspartocin, Antibiotic A-30912, Antibiotic A-1437, Antibiotic A-54145 or Antibiotic A-21978C.

9. The antimicrobial sulfonamide derivative of Claim 4 in which R is the core cyclic peptide of laspartomycin or aspartocin.

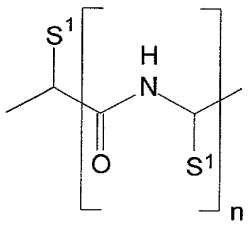
10. The antimicrobial sulfonamide derivative of Claim 4 in which R is the core antibiotic of laspartomycin or aspartocin.

11. The antimicrobial sulfonamide derivative of Claim 4 in which m is 1.

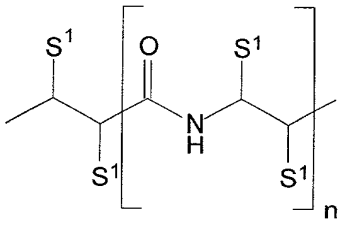
12. The antimicrobial sulfonamide derivative of Claim 4 in which R^1 and R^4 are hydrogen.

13. The antimicrobial sulfonamide derivative of Claim 4 in which L is selected from the group consisting of:

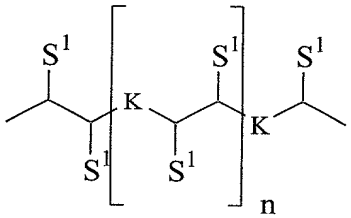
(L1)

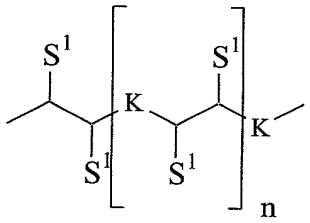


(L2)



(L3)



(L4) 

or a pharmaceutically acceptable salt or hydrate thereof, wherein:

n is 0, 1, 2 or 3;

each S^1 is independently selected from the group consisting of hydrogen, (C_1-C_{10}) alkyl optionally substituted with one or more of the same or different R^5 groups, (C_1-C_{10}) heteroalkyl optionally substituted with one or more of the same or different R^5 groups, (C_5-C_{10}) aryl optionally substituted with one or more of the same or different R^5 groups, (C_5-C_{15}) arylaryl optionally substituted with one or more of the same or different R^5 groups,(C_5-C_{15}) biaryl optionally substituted with one or more of the same or different R^5 groups, five to ten membered heteroaryl optionally substituted with one or more of the same or different R^5 groups, (C_6-C_{16}) arylalkyl optionally substituted with one or more of the same or different R^5 groups and six to sixteen membered heteroarylalkyl optionally substituted with one or more of the same or different R^5 groups;

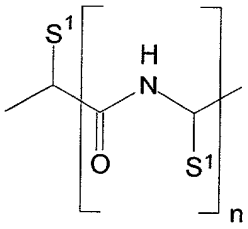
each R^5 is independently selected from the group consisting of —OR^6, —SR^6, —NR^6R^6, —CN, —NO_2, —N_3, —$C(O)OR^6$, —$C(O)NR^6R^6$, —$C(S)NR^6R^6$, —$C(NR^6)NR^6R^6$, —CHO, —R^6CO, —SO_2R^6, —SOR^6, —$PO(OR^6)_2$, —$PO(OR^6)$, —CO_2H, —SO_3H, —PO_3H, halogen and trihalomethyl;

each R^6 is independently selected from the group consisting of hydrogen, (C_1-C_6) alkyl, (C_5-C_{10}) aryl, five to sixteen membered heteroaryl, (C_6-C_{16}) arylalkyl and six to sixteen membered heteroarylalkyl; and

each K is independently selected from the group consisting of oxygen, nitrogen and sulfur.

14. The antimicrobial sulfonamide of Claim 13 in which each S^1 is independently a side-chain of a genetically encoded α-amino acid.

15. The antimicrobial sulfonamide of Claim 13 in which L is:



16. The antimicrobial sulfonamide derivative of Claim 15 in which each S^1 is independently a side-chain of a genetically encoded α-amino acid.

17. The antimicrobial sulfonamide derivative of Claim 15 in which n is 0.

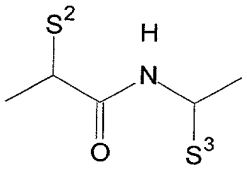
18. The compound of Claim 17 in which S^1 is hydrogen, Y^2 is decan-yl and R is the core cyclic peptide of aspartocin.

19. The antimicrobial sulfonamide derivative of Claim 17 in which S^1 is $-CH_2-CO_2H$, $-CH_2-CH_2-CO_2H$, $-C(OH)H-CONH_2$, $-CH_2-CONH_2$ or $-CH_2-CH_2-CONH_2$ or a salt or hydrate thereof.

20. The antimicrobial sulfonamide derivative of Claim 17 in which S^1 is $-CH_2$–indol-2-yl or $-CH_2$-phenyl.

21. The compound of Claim 20 in which R is the core antibiotic of laspartomycin and Y^2 is hexadecyl.

22. The antimicrobial sulfonamide derivative of Claim 13 in which L is:



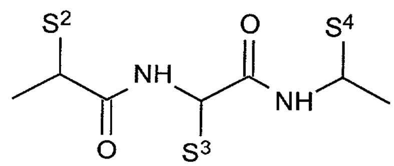
23. The antimicrobial sulfonamide derivative of Claim 22 in which S^2 and S^3 are

each independently a side chain of a genetically encoded α-amino acid.

24. The antimicrobial sulfonamide derivative of Claim 22 in which S^2 is hydrogen, $-CH_2$–indol-2-yl, $-CH_2-CONH_2$ or $-CH_2-CH_2-CONH_2$ and S^3 is $-CH_2-CO_2H$, $-CH_2-CH_2-CO_2H$ or a salt or hydrate thereof.

25. The antimicrobial sulfonamide derivative of Claim 22 in which S^2 is $-CH_2-CO_2H$, $-CH_2-CH_2-CO_2H$ or a salt or hydrate thereof and S^3 is $-C(OH)H-CONH_2$.

26. The antimicrobial sulfonamide derivative of Claim 13 in which L is:



27. The antimicrobial sulfonamide derivative of Claim 26 in which S^2, S^3 and S^4 are each independently a side chain of a genetically encoded α-amino acid.

28. The antimicrobial sulfonamide derivative of Claim 26 in which S^2 is $-CH_2$–indol-2-yl, S^3 is $-CH_2-CONH_2$ or $-CH_2-CH_2-CONH_2$ and S^4 is $-CH_2-CO_2H$, $-CH_2-CH_2-CO_2H$ or a salt or hydrate thereof.

29. The antimicrobial sulfonamide derivative of Claim 26 in which S^2 is $-CH_2$–indol-2-yl, S^3 is $-CH_2-CO_2H$, $CH_2-CH_2-CO_2H-$ or a salt or hydrate thereof and S^4 is $-CH_2-CONH_2$, $-CH_2-CH_2-CONH_2$ or $-C(OH)H-CONH_2$.

30. The antimicrobial sulfonamide derivative of Claim 4 in which m is 0.

31. The antimicrobial sulfonamide derivative of Claim 30 in which R^4 is hydrogen.

32. The antimicrobial sulfonamide derivative of Claim 30 in which R is the core

antibiotic of laspartomycin or aspartocin.

33. The antimicrobial sulfonamide derivative of Claim 32 in which R is the core cyclic peptide of laspartomycin or aspartocin.

34. A pharmaceutical composition comprising a compound according to Claim 4 and a pharmaceutically acceptable adjuvant, excipient, carrier or diluent.

35. A method for treating or preventing a microbial infection, said method comprising the step of administering to a subject a therapeutically effective amount of a compound according to Claim 4 or a therapeutically effective amount of a pharmaceutical composition according to Claim 34.

36. A method of inhibiting microbial growth, said method comprising the step of administering to a microbe an antimicrobially effective amount of a compound according to Claim 4 or an antimicrobially effective amount of a pharmaceutical composition according to Claim 34.

37. A method for making an antimicrobial sulfonamide derivative comprising sulfonylating an core antibiotic or core cyclic peptide with a lipophilic sulfonyl derivative, thereby providing a antimicrobial sulfonamide derivative.

38. The method of Claim 37 in which the lipophilic sulfonyl derivative is a activated lipophilic sulfonyl ester or a lipophilic sulfonyl halide.

39. The method of Claim 38 in which the activated lipophilic sulfonyl ester is a lipophilic hydroxybenzotriazole ester.

40. The method of Claim 39 in which the lipophilic sulfonyl halide is a lipophilic sulfonyl chloride.

41. A method for making an antimicrobial sulfonamide derivative comprising:

sulfonylating a linker with a lipophilic sulfonyl compound, thereby providing a lipophilic sulfonamide linker; and

covalently attaching the lipophilic sulfonamide linker to an core antibiotic or core cyclic peptide, thereby yielding a antimicrobial sulfonamide derivative.

42. A method for making an antimicrobial sulfonamide derivative comprising:

covalently attaching a linker to an core antibiotic or core cyclic peptide, thereby providing an linker core antibiotic or linker core cyclic peptide; and

sulfonylating the linker core antibiotic or linker core cyclic peptide with a lipophilic sulfonyl derivative, thereby yielding a antimicrobial sulfonamide derivative.